

LISTING OF THE CLAIMS:

1-6 (canceled)

7. (original) A method of determining the substrates of an E3 ligase, the method comprising:

introducing an E3 ligase coding sequence operably linked to an inducible promoter into a cell, wherein said cell is deficient in a negatively selectable enzyme;

introducing into a population of said cells a library of vectors comprising sequences encoding said negatively selectable marker fused to candidate E3 ligase substrate coding sequences;

induce expression of said E3 ligase in the presence of a compound toxic to cells expressing said enzyme;

wherein cells expressing said enzyme fused to a substrate for said E3 ligase are viable in the presence of said compound.

8. (original) The method according to Claim 7, further comprising the step of rescuing said candidate E3 ligase substrate coding sequences.

9. (original) The method according to Claim 7, wherein said rescue comprises specific PCR amplification.

10. (original) The method according to Claim 7, wherein said negatively selectable enzyme is thymidine kinase.

11. (original) The method according to Claim 7, wherein said E3 ligase is GRAIL.

12-24. (canceled)

25. (new) The method of Claim 7, further comprising confirming a candidate substrate by complementation in a two hybrid assay.